THE ANATOMY OF THE GASSERIAN GANGLION AND THE DISTRIBUTION OF PAIN IN RELATION TO INJECTIONS AND OPERATIONS FOR TRIGEMINAL NEURALGIA

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by

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JOHN HUNTER WAS well acquainted with that excruciating, spasmodic facial pain, or tic douloureux, which is now called trigeminal neuralgia. He wrote in a treatise on diseases of the teeth: " There is one disease of the jaws which seems in reality to have no connection with the teeth, but of which the teeth are generally suspected to be the cause. Operators have frequently been deceived by it, and even sound teeth have sometimes been extracted through an unfortunate mistake. I have known cases where all the teeth on the affected side have been drawn out and the pain has continued." He concluded that " the pain does not arise from any disease in the part but is entirely a nervous affection ".* Nearly 200 years later the cause of trigeminal neuralgia is still unknown, and healthy teeth are sometimes removed, but fortunately the pain can now be cured.

This study is the outcome of a recent follow-up of injections and operations for trigeminal neuralgia in 650 patients treated personally during 1946–63. It is concerned mainly with anatomical reasons for failures after Gasserian ganglion injections, and after operations, either of which should produce permanent cure.

It was found, firstly, that after " Gasserian ganglion " injections more than half the patients had some recovery of sensation, especially in the mandibular division; secondly, that mandibular nerve injections at the foramen ovale sometimes produced permanent anaesthesia in the first two divisions, but not in the third where the pain was situated; and, thirdly, that return of pain after fractional section of the sensory root was due to insufficient denervation, mostly during the earlier years before the anatomical behaviour of trigeminal neuralgia was properly appreciated.

Pain is the only manifestation of this mysterious disease, the aetiology and pathology of which remain obscure. It is well known from the natural history of the pain, both before treatment and after failed treatment, that it almost always increases in frequency and severity. As the disease does not shorten life, it is the more important permanently to

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* HUNTER, J. (1778) *A Practical Treatise on Diseases of the Teeth.* London, Johnson, p. 61.

abolish as soon as possible this curable pain, which can make old age so miserable, either by operation or by Gasserian ganglion injection, the choice depending upon circumstances in each patient and on the assessed limitation of each procedure. In order to prevent unnecessary suffering, permanent cure should not be unduly delayed by adopting temporary measures because the patient may later refuse further injections, or become unfit for operation, and is then committed to a life either of recurring injections which become increasingly difficult, or of drugs which are usually ineffective.

The pain is always stopped by anaesthetizing the affected area, and the relief is always permanent when central nerve-axon degeneration is produced either by cutting the sensory nerve root, or by injecting alcohol into the whole of the " Gasserian ganglion " (or more likely the sensory root). It is therefore disappointing when pain returns, either quickly or after several years. These procedures, especially operation, could with great benefit be used more often than they are but, before advising the possible guarantee of permanent cure, it is important to know, and be reasonably certain of avoiding, the causes of failure.

Injection of alcohol into or around the peripheral nerves, including, unintentionally, their intracranial portions in front of the Gasserian ganglion, relieves the pain only temporarily, for a year or two, because the nerves regenerate. Temporary relief is, of course, sometimes sufficient and preferable, e.g. when the patient is very old or unfit for operation, or during the first attack, or when pain is limited to the upper gum, or when total anaesthesia after Gasserian injection is undesirable (e.g. in the presence of cataract), or when the pain is bilateral. Medical treatment with analgesic tablets, for as yet there is no specific drug, may suffice when the attacks of pain are very infrequent, of short duration, and very mild.

" GASSERIAN GANGLION " INJECTIONS

The ganglion was always approached by the anterior route through the foramen ovale; the patient was supine and the head slightly elevated but not rotated. The needle entered the skin just lateral to the corner of the mouth, and was continued in a backwards and upwards direction, where the finger tip is conveniently pressed beneath the maxilla, towards a point 1 inch in front of the tragus of the ear, and with an inclination medially of about 15° towards the pupil of the eye. The base of the skull was identified for depth and the needle was then adjusted to find the foramen ovale, which was usually verified by a small injection of alcohol producing mandibular sensory loss. The needle was then continued in short stages of 2 to 3 mm. (Fig. 1) each followed by an injection of two or three drops of alcohol (1 drop = 0.015 c.c.), without preliminary novocain, until total sensory loss was obtained in all three divisions; a deeper injection then seemed unnecessary. The needle often had to be redirected, but it was

rarely advanced more than 10 to 15 mm. beyond the base of the skull, which, as post-mortem dissections have shown, was not deep enough always to reach the ganglion. Injections were made preferably against pressure, assumed to be inside the mandibular nerve or ganglion, but sometimes the needle must have been outside when a few drops went in suddenly and easily, presumably either in front of the ganglion (indicated by the broken line in Figure 1), or inside Meckel's cave, or into the middle fossa. Deep injections were avoided in order to reduce the risk of motor oculi nerve palsies, which were rare and transient, but the follow-up has shown that many injections were not deep enough for permanent anaesthesia.

There were 196 injections of alcohol (in altogether 165 patients) supposedly into the " Gasserian ganglion ", always with the intention of producing permanent anaesthesia in the whole trigeminal area; I never

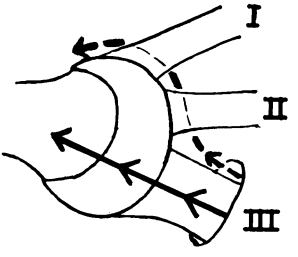


Fig. 1. Right Gasserian ganglion showing stages during the entry of a needle through the foramen ovale: inside the mandibular nerve, through the Gasserian ganglion (lateral part), into the sensory root. The broken line indicates spread of alcohol, from outside the mandibular nerve, medially in front of the ganglion.

felt able to inject only a selected part of the ganglion. In addition, 21 procedures (approximately 10 per cent) were abandoned without injection for various reasons, but mainly inability to enter the foramen ovale. Further attempts were sometimes refused, whilst in other patients they were sometimes successful. The foramen was never entered in 7 per cent of patients; this figure would probably have been less than 5 per cent if a second attempt had always been made. It is, however, much easier to pass the needle through the foramen than to be sure of entering the ganglion. Radiography was not used.

In this investigation into failures, and potential failures, the late results of injections have been assessed anatomically, on the extent and permanence of sensory loss when re-examined after one year or longer, which is the only certain criterion of permanent cure. Absence of pain is unreliable, because sometimes it fails to return soon after recovery of good sensation, but may do so later on.

Of the 196 injections, 81 per cent (to the nearest figure) produced total anaesthesia in all divisions (occasionally with sparing at the inner canthus), which, at the time, seemed satisfactory and it was hoped would remain

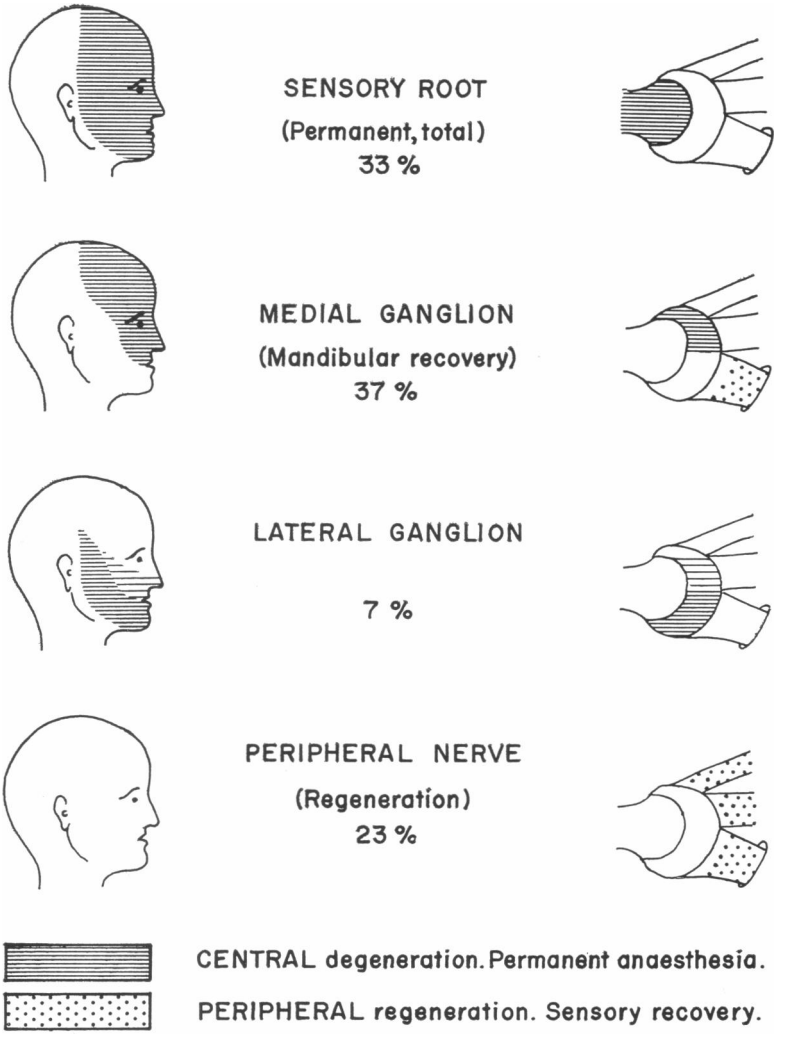


Fig. 2. Types of effect 1+ years after "Gasserian" injection in 86 patients. Left, the four types of final sensory loss; right, the presumed sites of action of alcohol.

permanently. Most of the other injections produced incomplete sensory loss which was sometimes permanently total in part of the trigeminal area and happened to be adequate depending upon the situation of the pain.

But, of 86 patients who were re-examined one year or longer after (the first) injection, only 33 per cent had total, or near total, anaesthesia, which was disappointing.

The four types of permanent effect after first injections, grouped according to the final pattern of sensory loss, are shown in Figure 2. There were also 35 followed-up repeat injections, for continued or recurrent pain, which are excluded because they nearly always reproduced the same previously unsuccessful result.

1. Sensory root effect

Only 33 per cent of patients had permanent total or near total (with inner canthus sparing) anaesthesia. Post-mortem injections, described later, showed that it is impossible to inject the whole ganglion, or even half of it, without affecting also the sensory root. It is assumed, therefore, that permanent total anaesthesia was due to alcohol in the sensory root, and that either the needle had been deeper than usual or the ganglion had been situated further forwards making the root more accessible. Alcohol was rarely injected after withdrawal of cerebro-spinal fluid (from Meckel's cave), which is perhaps one reason why only one-third of the patients are in this group.

2. Medial ganglion effect

In 37 per cent of patients there was unexpected return of normal or good sensation, sufficient to allow recurrence of pain, in the mandibular division only, whereas the total sensory loss in the first two divisions remained permanently. It is assumed that the temporary anaesthesia in the third division was an effect of alcohol on the mandibular nerve, and that the permanent loss in the first two divisions was due to alcohol somehow affecting the nerve cells in the corresponding part of the ganglion, or perhaps the medial half of the sensory root. It is, however, difficult to understand the frequent strictly peripheral nerve distribution of the total loss in the first two divisions (never in the first division alone) and of the sensory recovery in the third; only two patients showed graduated transition from total loss in the first division, through moderate loss in the second to slight loss in the third (which occurs more often after fractional sensory root operations).

In this group there were 16 repeat injections, all producing renewed mandibular anaesthesia, which, however, remained permanently after only two out of the 16. Such frequent, isolated mandibular regeneration was unexpected and it was difficult to understand why the lateral part of the ganglion, which is in continuity with the mandibular nerve, should so frequently be missed.

3. Lateral ganglion effect

It is perhaps not surprising, in view of the many patients in Group 2, that the reverse effect of total loss in the third division, usually partial loss

in the second, and normal sensation in the first, was uncommon, only 7 per cent. This was disappointing because of the frequent desire permanently to cure mandibular pain with preservation of sensation on the eye. The ganglion may have been close to, or on top of, the foramen ovale so that the needle immediately entered its lateral part (Fig. 13*c*).

4. Peripheral nerve effect

After 23 per cent of injections there was recovery of normal or good sensation in all three divisions, either rapidly within hours or days following transient nerve block, especially in the first and second divisions, or later by regeneration after 12–18 months. It must be assumed that the alcohol affected the nerves in front of the ganglion. Pain, of course, frequently recurred and, as in Group 2, repeat injections were usually again followed by return of sensation. This was the worst group; permanent anaesthesia was obtained in only three of 12 patients who had 17 repeat injections, i.e. they had altogether 29 injections only three of which produced final total anaesthesia. The needles evidently had not reached the ganglion.

Occasionally in Groups 1 and 2, and before sensation returned in Group 4, there was sparing of normal or moderate sensation in a half-circle about 1 inch at the inner canthus of the eye which is easily missed on examination because the forehead is anaesthetic. This small area of remaining sensation, innervated presumably from the medial end of the ganglion, is unimportant unless the pain is situated around the orbit or up the nose; in several such patients pain recurred at the inner canthus. This area is sometimes difficult to anaesthetize by further injections, but it is easily denervated by operation.

Multiple injections

There were 35 followed-up repeat injections (in 22 patients), only 14 per cent of which produced permanent anaesthesia; the others merely reproduced the same pattern of temporary sensory loss. Permanent anaesthesia was obtained in only two of the nine patients who had three or four injections; both were at the fourth attempt and at greater depth.

It appears, therefore, that many " Gasserian " injections had been in front of the ganglion, and it is probable that if, routinely, they had been made more deeply into the sensory root, after withdrawing cerebro-spinal fluid, more patients would have had permanent anaesthesia. The results were worst in patients with third division pain because of the frequent recovery of mandibular sensation. The striking difference between the ease in obtaining a permanent result in some patients and the great difficulty or impossibility in others could hardly be due entirely to technique because all injections had been made by one person; an anatomical explanation seemed more likely.

The late results from the patients' standpoint of relief of pain were, however, better than might be expected from the anatomical sensory loss, as 65 per cent of patients (56 out of 86) remained free of pain for 1–17 years after injection; in 55 per cent the area of persisting total anaesthesia adequately covered the pain zone and the cure may be regarded as permanent, and 10 per cent were still free of pain although sensation had returned. Nearly half the recurrences (14 out of 30) started within 12 months, 24 started within three years and the longest interval was seven years, whilst 23 patients remained free of pain for 7–17 years.

MANDIBULAR NERVE INJECTIONS

Injections into the mandibular nerve at the foramen ovale, for pure third division pain, are normally followed by recovery of sensation and usually the pain returns. Although not expected to produce permanent cure, they are relevant to the present discussion because alcohol may spread accidentally to the maxillary and ophthalmic nerves, and occasionally affects also the medial half of the ganglion; in such patients (and also in patients in Group 2 Gasserian injections) it had frequently been noted that the foramen ovale was large and easily entered, and that mandibular sensory loss was often only partial. The needle was probably partly or entirely outside the nerve, and as more alcohol was injected it produced the same effects (Fig. 3) as after Gasserian injections; but the relative incidence was different because the needle was situated, on average, probably 10 mm. or more further forwards. Sometimes, the first two or three drops of alcohol went in suddenly, without resistance, and immediately produced total sensory loss in the first two divisions and perhaps only partial loss, or no loss, in the third.

The final results of the 164 followed-up injections fall into two groups:

(*a*) 67 per cent produced, as intended, mandibular anaesthesia alone, followed later by return of sensation.

(*b*) The remaining 33 per cent produced sensory loss also in the first and second divisions.

Compared with Gasserian injections, the sensory root effect was rare, in only one patient, presumably because the needles were farther away. On the other hand, temporary peripheral nerve effects from alcohol in front of the ganglion were considerably more frequent than permanent medial ganglion effects, instead of less frequent as after Gasserian injections; they occurred in two-thirds of the patients in whom alcohol had spread intracranially, but often were only transient, disappearing within a day or so. The medial ganglion effect was much less frequent than after Gasserian injections, and the lateral ganglion effect was rare after both injections. Thus, during difficult mandibular injections, alcohol frequently spread to the other nerves, or the ganglion, producing the same

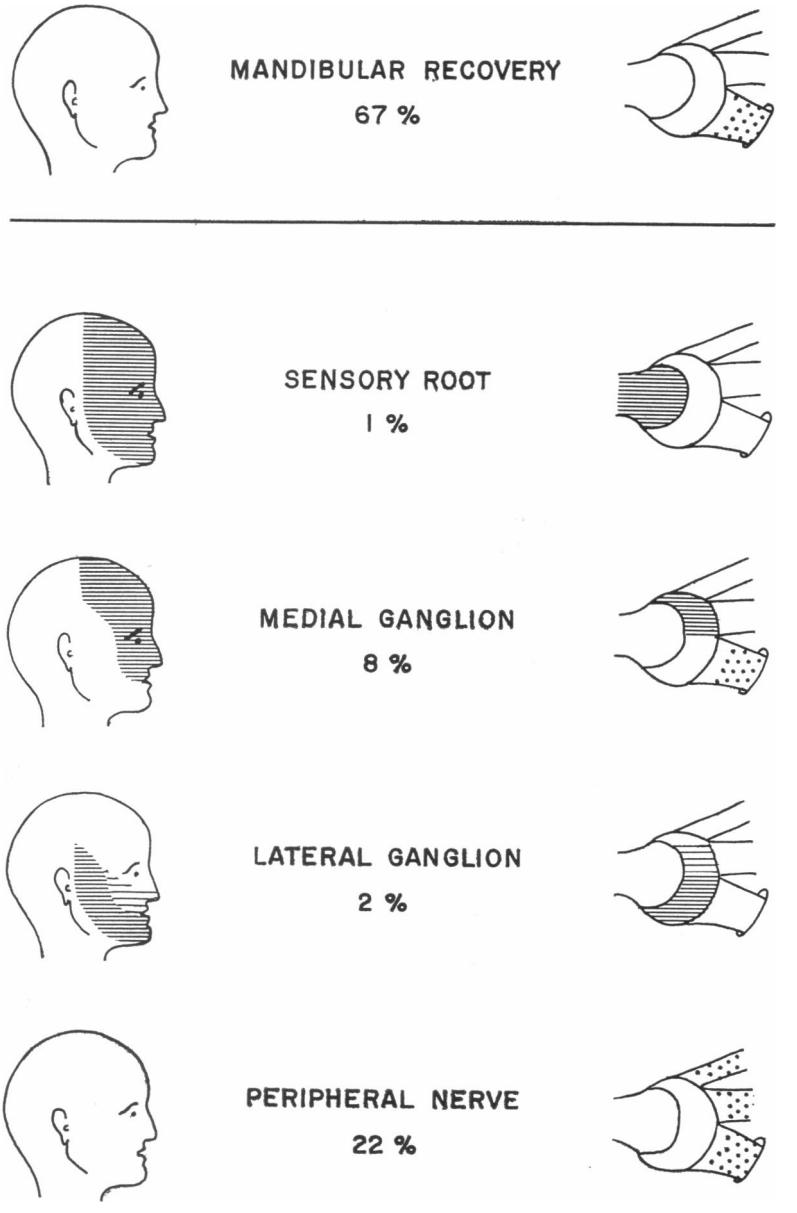


Fig. 3. Types of effect 1+ years after mandibular injection at the foramen ovale in 164 patients. Left, the types of final sensory loss; right, the presumed sites of action of alcohol.

effects as during incomplete Gasserian injections that were not sufficiently deep, but it almost never reached the sensory root. Immediate total sensory loss in the first two divisions remained permanently more often after Gasserian injections, in which usually more alcohol was injected in an attempt to obtain total anaesthesia in the third division, than after mandibular injections which were immediately stopped when sensory loss appeared in the other divisions.

The occurrence of the same effects after injections at the foramen ovale, or deeper in the region of the ganglion, raised two questions about Gasserian injections: (1) why the lateral part of the ganglion, which is in continuity with the mandibular nerve and more in the line of the needle, was often difficult to inject; and (2) why permanent sensory loss occurred more often in the first two divisions, in 70 per cent (33 + 37) of patients, than in the third division, in only 40 per cent (33+7); and why it sometimes occurred after mandibular injections when the needle was thought not to have entered the skull, and was most unlikely to have reached the medial part of the ganglion. Anatomically, these findings were difficult to understand, and clinically they were unfortunate because pain occurs most frequently in the third division. In an attempt to answer these questions various dissections and injections were carried out in 100 bodies.

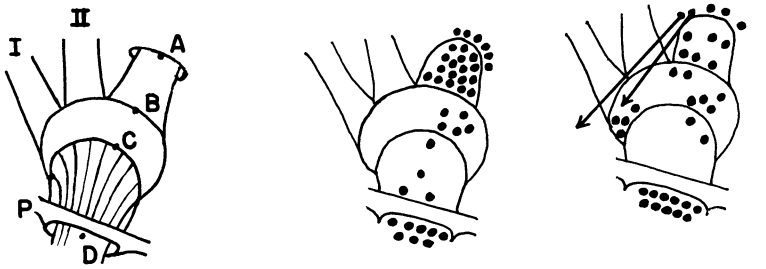
POST-MORTEM DISSECTIONS AND INJECTIONS

The Gasserian ganglion lies in a hollow of variable depth on the apex of the petrous bone and the foramen lacerum, and sometimes also on the posterior lip or floor of the foramen ovale; its medial part lies on the cavernous sinus. The ganglion is crescentic as seen both from its upper surface and also in sagittal section as a result of which the sensory root emerges through a deep hilum on its posterior aspect. The sensory root continues backwards and upwards through the trigeminal opening, under the petrosal sinus, into the posterior fossa. The ganglion is longer, thinner and more curved, sometimes even horse-shoe in shape, than is usually shown in anatomical illustrations. It is 4 to 5 mm. wide and only 2 to 4 mm. thick, and as it is 15 to 25 mm. long it is unlikely that alcohol injected into it could infiltrate far without bursting through its concave posterior border into Meckel's cave. The mandibular part occupies approximately half the ganglion.

A small narrow spur of bone rarely (4 per cent) projected from the floor of Meckel's cave upwards between sensory root bundles, without constant relationship to the peripheral divisions. It never joined the roof, and the cave was not divided into compartments. Spurs are too rare to affect the overall results of injections, and are not likely to cause error when the cave is opened through the roof during intradural operations.

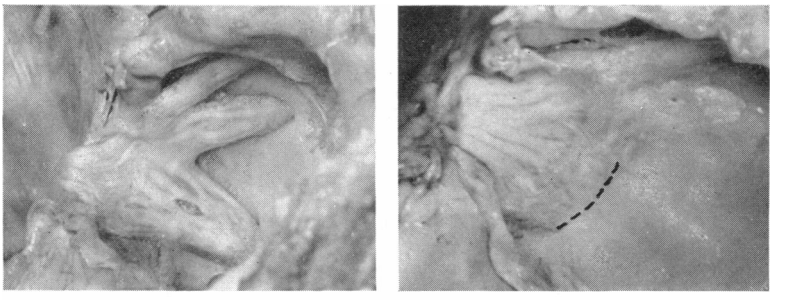
The length of the mandibular nerve from A, at the antero-superior margin of the foramen ovale, to B (Fig. 4*a*) varied as follows:

15 short nerves (pre-fixed ganglion)	of 0 to 3 mm.
60 average nerves	4 to 7 mm.
25 long nerves (post-fixed ganglion)	8 to 10 mm.



(*a*) (*b*) (*c*)

Fig. 4. (*a*) Gasserian ganglion measurements. Mandibular nerve (AB) 0-10 mm.; ganglion width (BC) 5 mm.; sensory root (CD) 5-15 mm. The petrosal sinus (P) is shown crossing the trigeminal opening. Sites of emergence of needles: (*b*) first punctures; (*c*) after redirection towards the trigeminal opening or towards the medial part of the ganglion.



(*a*) (*b*)

Fig. 5. Post and pre-fixed ganglia. (*a*) Post-fixed ganglion with a long mandibular nerve of 10 mm., through which a needle is projecting, and a short sensory root of only 5 mm. (*b*) Pre-fixed ganglion covering foramen ovale (anterior margin outlined) without visible mandibular nerve, and long sensory root (cut short).

The variation of 10 mm. must influence the results of Gasserian injections, e.g. a needle at an average depth of, say, 7 to 8 mm. behind the anterior margin of the foramen may be behind, within, or in front of the ganglion (Fig. 5). To be sure of reaching the sensory root the needle must be introduced at least 15 mm. beyond A, or about 25 mm. from the base of the skull allowing 10 mm. for the foramen ovale canal (Figs. 6 and

13). It is clear that many injections had not been deep enough to reach the sensory root or the ganglion.

The length of the sensory root from C to D, on the petrous ridge at the trigeminal opening, varied as follows:

14 short sensory roots (post-fixed ganglion)	of 5 to 7 mm.
80 average sensory roots	8 to 12 mm.
6 long sensory roots (pre-fixed ganglion)	13 to 15 mm.

The variation of 10 mm. is important in middle fossa operations, because a long root facilitates the accurate selection and division of the separate nerve root bundles during fractional section. When the root is short it is

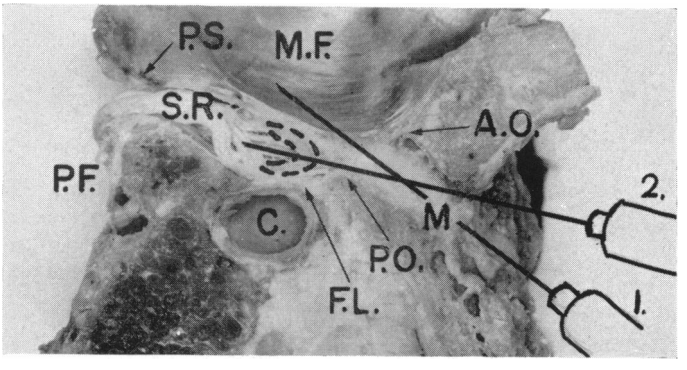


Fig. 6. Vertical section of right petrous bone (along line A in Fig 13*a*), through Gasserian ganglion (outlined) and the foramen ovale. Sensory root (SR); mandibular nerve (M); middle fossa (MF); posterior fossa (PF); carotid artery (C); petrosal sinus (PS); foramen lacerum (FL); anterior (AO) and posterior (PO) margins of the foramen ovale. Needle (1) along the mandibular nerve misses the ganglion in a deep hollow; needle (2) at a lower angle, obliquely through the foramen ovale, enters the sensory root (× 1.8).

difficult to see the bundle that enters the lateral end of the ganglion, or sometimes appears to penetrate the dura behind the ganglion; also, the dural opening over the sensory root may be partly over the (post-fixed) ganglion.

Bone measurements from the petrous ridge to the anterior margin of the foramen ovale, from D to A, varied from 16 to 26 mm., depending on the size of the head, and on the development of the foramen ovale and the variable size of its anterior margin; the latter affected the shape and obliquity of the foramen, making it rounder or narrower. The distance from the petrous ridge to the postero-inferior margin of the foramen, which forms the anterior boundary of the foramen lacerum, was less variable, 12 to 18 mm. Although there was no fixed relationship between ganglion and bone, the anterior border of the ganglion was usually within 2 mm.

in front of, or behind, the posterior lip of the foramen ovale, but in 8 per cent it was 3 to 4 mm. anterior, lying on the floor of the foramen, and in 7 per cent it was 3 to 4 mm. posterior.

As regards depth of injection that will with safety always reach the sensory root, the longest distance of 15 mm. (A to C) was about the same

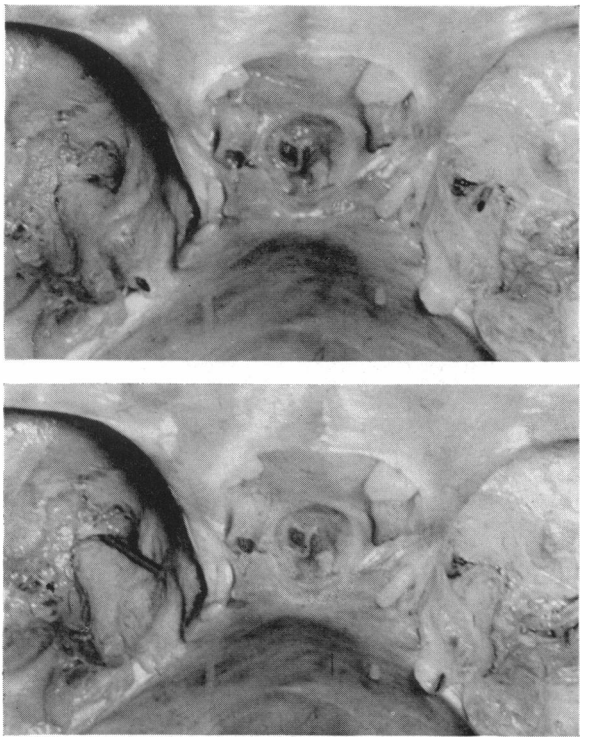


Fig. 7. Needles in various positions. Above, first punctures, the needle on the right passing upwards at the foramen ovale, missing the mandibular nerve; and on the left in the sensory root. Below, the same needles redirected, on the right into the sensory root, and on the left one of the few instances in which it was possible to redirect the needle towards the medial ganglion (and cavernous sinus).

as the shortest bone distance of 16 mm. to the petrous ridge (A to D) beyond which a needle might pass through the trigeminal opening into the posterior fossa. The optimum depth is thus limited narrowly to about 25 mm. from the base of the skull, but, assuming that alcohol injected into the ganglion bursts into Meckel's cave (see page 364), the depth could be reduced to about 20 mm.

Direction of needle. Trigeminal needles were introduced through 40 foramina, using the same skin entry and direction as in patients. The

needles were continued until they appeared either through the trigeminal opening into the posterior fossa (the ideal direction for sensory root injections), or, when pointing more upwards, through the dura into the middle fossa. The dura was then stripped forwards off the ganglion, and the site of emergence of each needle from the mandibular nerve, ganglion or sensory root was charted (Fig. 4*b* and *c*). During this series, one other attempted introduction was impossible owing to the presence of a pterygospinous bar of bone across the lower opening of the foramen ovale, and

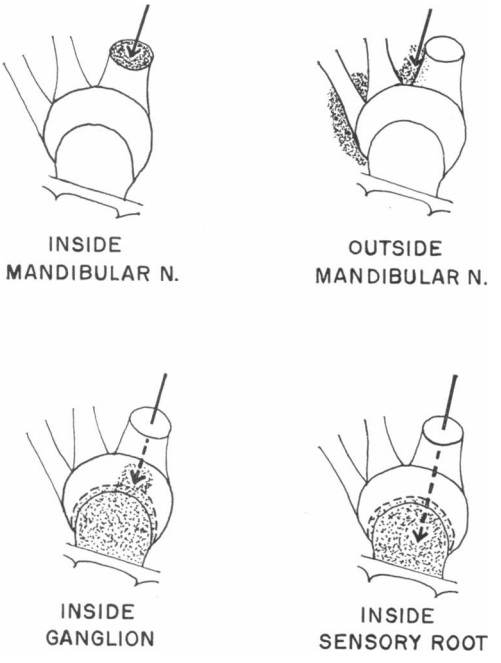
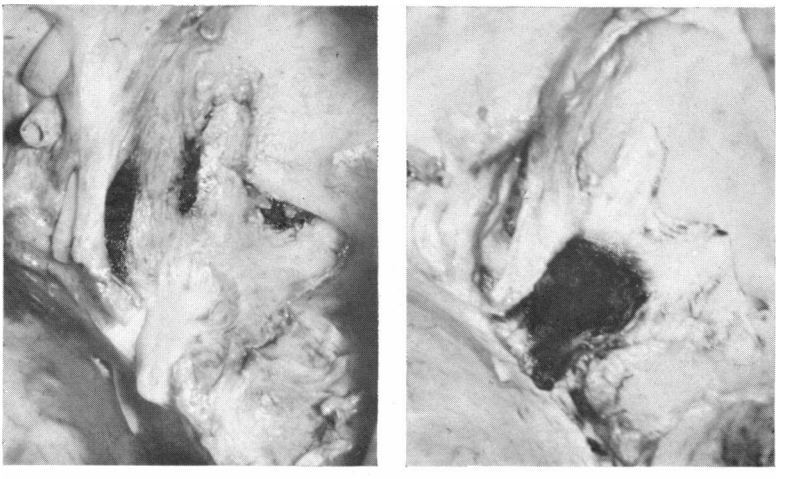


Fig. 8. Diagrams of post-mortem injections showing the four patterns of distribution of dye, depending upon the position of the needle.

two others failed until after the needles had been passed in the reverse direction from inside the skull.

Of the first attempts (Fig. 4*b*) 12 needles entered the sensory root and eight of them continued through the trigeminal opening. The other 28 needles had been directed too much upwards, and they emerged either from the ganglion, missing the sensory root; or, more often, further forwards from the mandibular nerve in front of the ganglion; and sometimes they passed steeply upwards at the foramen ovale, outside the mandibular nerve. No needle went to the medial part of the ganglion.

Needles usually enter the foramen ovale most easily at a fairly steep angle, but they are then more likely to continue upwards in front of the ganglion, especially when the mandibular nerve is long (Fig. 6). In order to enter the thin ganglion, and the sensory root behind it, the angle of the needle should be kept low by entering the skin of the cheek as high as possible and passing obliquely through the foramen. This is sometimes difficult because of the variable direction of the foramen and the variable slope of the middle fossa; when the upper surface of the petrous bone is unusually steep, the needle may strike bone under the ganglion, especially in a small skull. On the other hand, the needle may pass over a ganglion that lies in a deep hollow.



(*a*) (*b*)

Fig. 9. Right Gasserian ganglia *in situ* after injection of violet alcohol and reflection of dura. (*a*) Dye extending antero-medial to the ganglion after injection outside the mandibular nerve at the foramen ovale; there is no dye lateral to the ganglion or in the sensory root. (*b*) Injection into the sensory root filling Meckel's cave; the ganglion is unstained except a strip along its concave posterior border.

The needles that had emerged too far forwards, in front of or through the ganglion, were then re-introduced through a higher skin entry, 1 to 2 cm. above the level of the mouth, in a more horizontal direction skirting the lower border of the maxilla, to see if they could be made to enter the sensory root (Fig. 4*c*). This often succeeded, even when they had previously emerged far forwards at the foramen ovale. Other needles could not be lowered sufficiently to enter Meckel's cave, nor occasionally even the ganglion, and three needles still emerged from the foramen outside the nerve. Injections into the ganglion would probably have burst backwards into Meckel's cave (see page 364), thus leaving only a few cases in which apparently it would be impossible to inject alcohol into the sensory root.

In addition, attempts were usually made to redirect the needles towards the medial part of the ganglion by entering the skin further laterally. This was often prevented by the ramus of the mandible, and it was achieved with only six needles, two of which were separated by dura from the ganglion (Fig. 4*c*). It is therefore unlikely that the frequent medial ganglion effects of Gasserian injections were due to injections actually into the medial part of the ganglion. Needles in various positions are shown in Figure 7.

Thus, with a high skin entry, the majority of needles will enter Meckel's cave if they are advanced deep enough to allow for possible post-fixation of the ganglion; it is very difficult to enter the medial part of the ganglion.

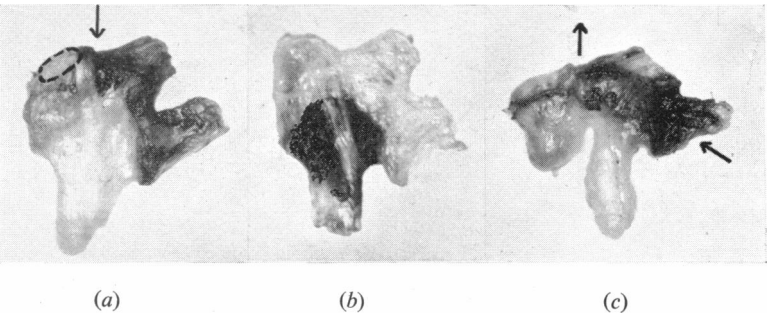


Fig. 10. The deep surface of right ganglia. (*a*) After anterior injection outside the short mandibular nerve (outlined) showing staining along the front of the medial half of the ganglion and on the maxillary and ophthalmic nerves, but not laterally. (*b*) After injection into the sensory root (specular high lights touched out). (*c*) After injection into the cavernous sinus (from inside the skull) showing also a small branch from the ovale emissary sinus continuing under the mandibular nerve.

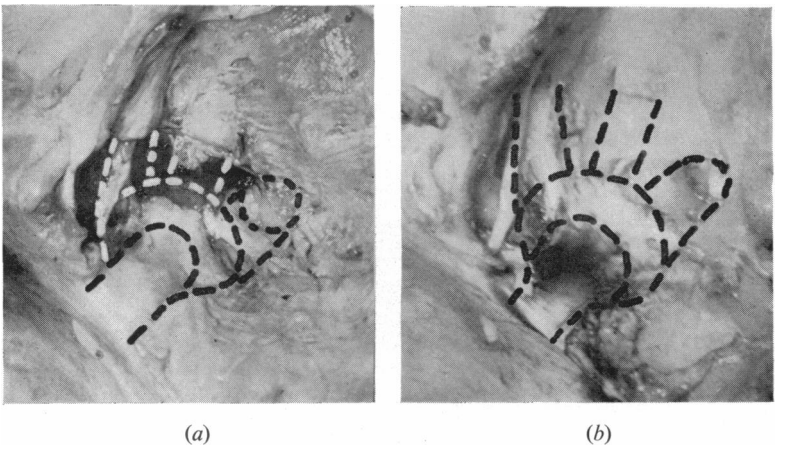
Injection of dye. Eighty Gasserian or mandibular injections were made through the foramen ovale, usually after the brain had been removed, using either 6 per cent charcoal in mucilage or, more often, a saturated filtered solution of cresyl-violet in absolute alcohol to resemble the material used in patients. The dura was then stripped forwards off the ganglion. The quantity injected was usually 3 to 5 min., occasionally 10 or 15 min. (1 min. = 0.06 ml.). Coloured alcohol was more informative than charcoal, and frozen histological sections showed that it often penetrated the nerves and sometimes the ganglion.

There were four main patterns of distribution of dye, depending upon the position of the needle (Fig. 8).

1. A small injection, against pressure, inside the mandibular nerve coloured the whole thickness of the nerve and was retained within it.

2. When the needle was outside the mandibular nerve the dye often spread medially, deep to the maxillary and ophthalmic nerves, along the

front of the ganglion to its medial end (Figs. 1, 9*a*, 10*a*, 11*a*). The dye had entered a dural channel, the lateral end of which passed downwards through the foramen ovale on the medial side of the mandibular nerve (Figs. 12, 13*d*); the upper end continued medially, on the foramen lacerum and the bone in front, deep to the junction of the maxillary nerve and ganglion (Fig. 13*e*, *f* and *g*). The dye crossed the fibrous band attached to the lingula of the sphenoid, then widened and extended posteriorly under the ophthalmic nerve and adjoining ganglion (Fig. 13*h*) to beyond the postero-medial border of the nerve, near the dorsum sellae. The channel appeared to have communicated with the cavernous sinus, and the carotid artery was stained; after a large injection, dye continued into the petrosal sinus and under the dura on the basi-sphenoid. The wall of the channel



(*a*) (*b*)

Fig. 11. Dye on the right middle fossa after removal of the ganglia (outlined). (*a*) Dye extending medially from the foramen ovale (cut surface of mandibular nerve is unstained) to the cavernous sinus; the floor of Meckel's cave is unstained. (*b*) Dye on the floor of Meckel's cave after injection into the sensory root; no dye anteriorly. The abducens nerve is seen crossing the carotid artery.

and the dural sheath of Meckel's cave prevented dye from extending to the sensory root. Sometimes a thin line of dye extended laterally under the mandibular nerve in a variable, usually small, branch of the channel (Fig. 10*c*) to middle meningeal veins in the middle fossa, or to the foramen spinosum, but not around the lateral side of the ganglion which was adherent to dura and usually remained unstained. Dye never spread over the superior surfaces of the maxillary or ophthalmic nerves or over the medial part of the ganglion, all of which were adherent to dura, but it was sometimes seen in a small space on the upper surface of the mandibular nerve and the adjoining part of the ganglion.

Dye in this anterior distribution was sharply demarcated and constant, and it occurred many times. The stained channel was not a potential

space opened by the pressure of injected fluid because it was present in skull bases removed intact and sawn vertically through the ganglion after fixation without previous injection (Fig. 13*e*). The probability that the channel was a venous sinus, and that alcohol had in fact entered the cavernous sinus without opening an artefact, at first seemed doubtful because it was empty of blood on dissection. After removal of the brain, however, blood normally drains away from the small dural sinuses, but in one body, after death from congestive heart failure, vertical section through the petrous bone showed blood in the channel (Fig. 13*g*). The channel was examined histologically, and was found to be a split in the dura, its wall consisting of a thin layer of dura (very thin on the maxillary nerve) lined by endothelium, similar to other venous sinuses; it was not a vein. It thus

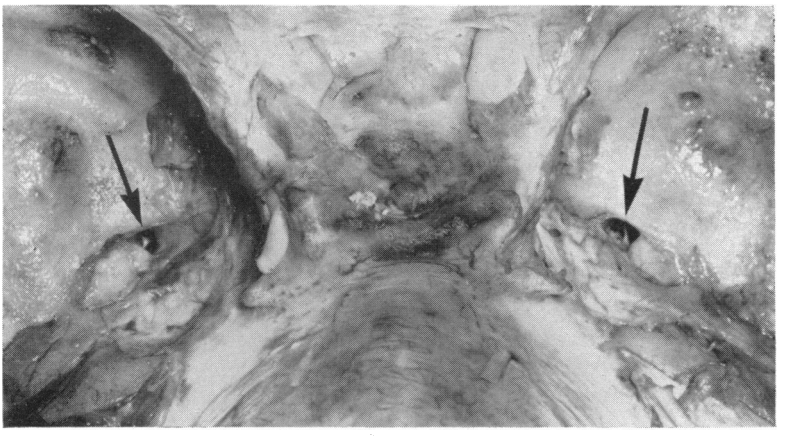


Fig. 12. The middle cranial fossa after removal of both ganglia showing a large venous sinus passing downwards through each foramen ovale on the medial side of the cut mandibular nerve.

became evident that the channel, which appeared to be always present, was a dural venous sinus that extends laterally from the cavernous sinus and leaves the skull through the foramen ovale to join the pterygoid plexus of veins. This leads to the surprising conclusion that during injections, at or just above the foramen ovale, alcohol may be injected into a venous sinus and may enter the cavernous sinus. Free communication between the two sinuses was proved by injecting violet alcohol into the cavernous sinus postero-medial to the ophthalmic nerve; the dye went along the venous (ovale emissary) sinus and down through the foramen ovale, staining the same part of the ganglion and nerves (Fig. 10*c*) as during injections at the foramen ovale, and it also entered the petrosal sinuses but not Meckel's cave. Clinically, there was never any evidence of sinus thrombosis which might be expected to occur if alcohol entered a sinus and perhaps continued slightly into the cavernous sinus.

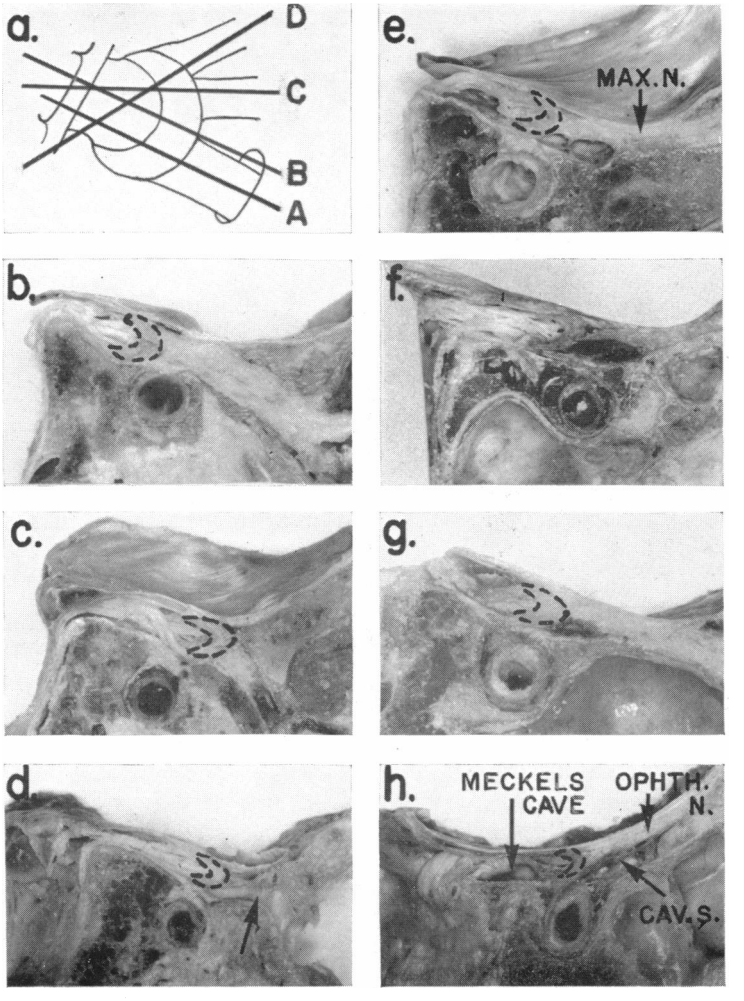


Fig. 13. Vertical sections (× 1.3) through petrous bones along the lines shown in (*a*); the ganglia are outlined. Sections along A are seen in (*b*) showing a relatively post-fixed ganglion; and in (*c*) showing a pre-fixed ganglion at the foramen ovale. Section along B is seen in (*d*) showing the venous sinus extending from under the front of the ganglion forwards and downwards through the foramen ovale. Sections along C, showing the venous sinus under the maxillary nerve and the front of the ganglion, are seen in (*e*) with the sinus empty; in (*f*) with the sinus containing dye after injection at the foramen ovale; and in (*g*) with the sinus containing blood. Section along D is seen in (*h*) showing the cavernous sinus, ophthalmic nerve and Meckel's cave.

3. Injections into the ganglion were always in its lateral (mandibular) part. The dye in the ganglion was limited to a small area around the needle point, and it burst through the concave posterior border into Meckel's cave and usually stained all the root bundles; this may be one reason why the lateral ganglion type of sensory loss was uncommon. Dye never burst through the front of the ganglion, and the three nerves were unstained.

4. When the needle had continued through the ganglion into the sensory root, a small injection filled Meckel's cave and deeply stained all the root bundles (Figs. 9*b*, 10*b* and 11*b*). Anteriorly, the dye was confined by the attachment of the dura of Meckel's cave around the whole length of the upper and lower surfaces of the ganglion near its posterior border which was stained. The front of the ganglion, the nerves and the venous sinus were unstained.

It is believed that the naked-eye distributions of the dye show where alcohol acts in producing the different clinical effects of Gasserian and mandibular injections; that injections filling Meckel's cave produce, as is well known, permanent total sensory loss; that alcohol injected into the ganglion probably always spreads into the sensory root; and that alcohol anteriorly in the venous sinus (which must occur frequently in patients) and in, or alongside, the mandibular nerve produces the peripheral nerve effects, and probably also the medial ganglion effects, although histological proof of the latter was not obtained.

As regards the mechanism of the last two effects, it is assumed that peripheral nerve effects must always be due to alcohol in front of the ganglion, and, as dye anteriorly was always inside the venous sinus, alcohol presumably penetrates directly into the ophthalmic and maxillary nerves where they lie in the thin walls of the cavernous sinus and the ovale emissary sinus respectively.

Medial ganglion effects are almost certainly not due to injections into the medial half of the ganglion because it is difficult to direct a needle point to that part of the ganglion (a needle directed through the medial side of the foramen ovale is more likely to enter the venous sinus). The probability that they result from alcohol anteriorly in the venous sinus, rather than posteriorly in Meckel's cave, is supported by the follow-up in patients which showed that the sensory loss always involved the first two divisions and never the first alone, that it usually had a strictly peripheral nerve distribution, and that it occurred also during mandibular injections which were unlikely to reach Meckel's cave (and had produced permanent total trigeminal anaesthesia in only one patient). The staining on the front of the ganglion suggested that permanent sensory loss in the first two divisions might be due to penetration of alcohol directly into the ganglion. If this occurs, involvement of the medial part of the ganglion,

in addition to the ophthalmic and maxillary nerves, may depend partly upon its antero-posterior position, in relation to the foramen ovale and the venous sinus, but it is more likely to depend upon the quantity of alcohol injected; the latter would explain the more frequent medial ganglion effects during difficult Gasserian injections, when more and more alcohol was apt to be used, than during mandibular injections which were stopped immediately sensory loss appeared in the first two divisions. The amount of alcohol in the sinus, and the out-flow of blood, probably determine the incidence of transient nerve block or nerve degeneration or permanent medial ganglion involvement.

It is not known how alcohol spreads in the cerebro-spinal fluid inside Meckel's cave. A small slow injection of absolute alcohol (specific gravity 0.79) may rise in the cerebro-spinal fluid (specific gravity 1.007) and affect only the root bundles from the highest part of the ganglion, which is the medial part when the head is supine, or slightly elevated, but not rotated; this would perhaps occur more easily if alcohol entered the fluid space beneath the medial half of the sensory root. The antero-lateral part of the root, on the other hand, is slightly adherent to the floor of the cave, and, although it is at a lower level, a small injection into it may tend to remain localized and produce a lateral ganglion type of sensory loss. Meckel's cave, however, is small, and alcohol probably diffuses freely and affects all the root bundles.

Uncertainty about the movement of alcohol inside Meckel's cave makes it difficult to assess the importance of positioning the head during injections. In order to limit the action of floating alcohol to the lateral half of the sensory root, the head would need to be turned markedly to the opposite side because the medial part of the ganglion slopes upwards at an angle of at least 45°. No attempt had been made in patients, by turning the head, to restrict sensory loss to the second and third divisions.

Attempts to demonstrate histologically the presence of dye inside the ganglion were successful in the case of posterior (root) injections but failed in the case of anterior injections. Frozen sections after injection into Meckel's cave showed good violet staining of the root bundles and of the nerve cells throughout the ganglion, proving that alcohol had penetrated into the ganglion (Fig. 14). Alcohol extended further inside the ganglion than on the surface, where it was limited by dural attachments. Permanent sensory loss after injection into Meckel's cave is therefore due to the effect of alcohol either on the nerve fibres in the sensory root, or on the nerve cells in the ganglion, or both, depending upon their vulnerability. It was, however, not possible to demonstrate similar penetration of dye from the venous sinus through the front of the ganglion into nerve cells, apart from staining of a few cells near the surface. The easier penetration of alcohol from Meckel's cave may be facilitated by the numerous small rootlets, whereas anteriorly the dye must pass through the thin wall of the sinus,

and the entry area is reduced by the large compact nerves and is limited to the lower surface of the front of the ganglion.

Dye frequently penetrated through the first few millimetres of the maxillary and ophthalmic nerves where the staining was easily seen naked-eye, and histologically it was sometimes visible also along the fascicles of these nerves across the width of the ganglion. The effect of alcohol may extend further than the visible dye, and from the venous sinus it may reach and damage all the ganglion cells that supply the ophthalmic and maxillary nerves. Another (and more likely) possibility is that alcoholic damage to peripheral nerve fibres at their junction with the ganglion produces irreparable retrograde degeneration of the ganglion cells. Either mechanism would explain the limitation of permanent sensory loss to the distri-

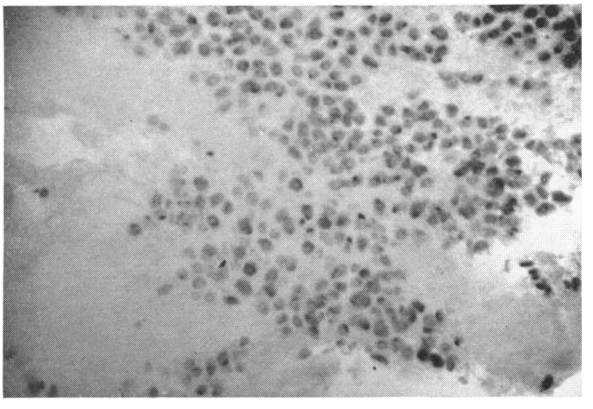


Fig. 14. Unstained frozen section of ganglion showing cresyl-violet inside the nerve cells after penetration from Meckel's cave.

bution of the two nerves. In patients with medial ganglion or peripheral nerve effects, the mandibular sensory loss (which initially was sometimes only partial) usually recovered, possibly because the mandibular nerve is thicker, alcohol is less often in contact with the lateral part of the ganglion, and many of the ganglion cells are farther away.

It is not clear why sensation sometimes remained at the inner canthus. It resulted presumably from sparing of the medial tip of the ganglion or of the most medial nerve bundle in the sensory root, possibly when the ganglion was unusually curved or horse-shoe in shape. When too little sensory root had been spared during lateral fractional section operations, the residual ophthalmic sensation was similarly maximal at the inner canthus.

The abducens nerve was sometimes stained in the cavernous sinus, where it lies on the deep surface of the ophthalmic nerve (Fig. 11*a*);

it is possible that abducens palsies, of which there were two after 196 Gasserian and two after 208 mandibular injections, occurred only when alcohol entered the cavernous sinus. The oculo-motor nerve was never stained, possibly because the dye was mainly in the lower, dependent part of the cavernous sinus; it is uncertain whether the six palsies after Gasserian and only one after mandibular injections were caused by alcohol in the cavernous sinus, or occurred when the needle had entered the middle fossa and alcohol in the cerebro-spinal fluid reached the nerve above the cavernous sinus.

Clinically, during Gasserian injections it is impossible to know whether sensory loss has resulted from the action of alcohol in the sensory root and will remain permanently, or in front of the ganglion and will be followed by partial or complete regeneration. Because of the unknown position of the ganglion, and of uncertainty about the exact position of the needle, the final results of Gasserian injections must always remain in doubt for a year or two to allow time for regeneration, unless cerebro-spinal fluid had been withdrawn, indicating the probability of injection into Meckel's cave. It is evident that in many patients sensory loss had unfortunately been produced, most likely by injection into the emissary venous sinus, before the needle was deep enough to have entered the ganglion or sensory root.

SENSORY ROOT OPERATIONS

For permanent cure, operation was always preferred to ganglion injection when there was no contra-indication to general anaesthesia. There were 246 operations (in 241 patients) on the sensory root, nearly all fractional sections, with six post-operative deaths—a mortality rate of 2.5 per cent (there have now been 76 operations since the last death). This mortality is too high, but five of the patients had a long history of pain treated conservatively until further injections were refused and the risks of cardio-vascular disease had then to be accepted, whereas earlier operation might well have been safe. As the fatalities were due to the patient's general condition, and not to operative damage in the vicinity of the nerve root, the mortality rate can be kept low by careful selection, and the relatively small risk in older patients may sometimes reasonably be accepted because of the greater likelihood of permanent cure after operation than after Gasserian injection.

Fourteen operations were abandoned, without cutting the sensory root, usually because the approach was hindered by abnormal vessels passing between the temporal lobe and the middle fossa, or, occasionally, because the nerve root was partially obscured by troublesome venous bleeding from the cut edge of the dura. Small vessels between the temporal lobe and dura may safely be divided, but the sacrifice of larger veins in old patients is apt to produce temporal lobe oedema; in order to avoid this

risk there should be no hesitation in abandoning the operation in favour of either cutting the nerve root in the posterior fossa or trying Gasserian injection.

The pain is always abolished by cutting the whole sensory root in the posterior fossa, which is routine in some clinics, but I always preferred the old fractional section operation, in the middle fossa, cutting sufficient sensory root to anaesthetize the affected area; this preserves some valuable sensation, either on the eye or in the mouth, and reduces the area of numbness. Operation was usually immediately successful; out of 158 patients who were re-examined there were only five early failures with continuation or recurrence of pain within 12 months, but pain sometimes returned after several years. There were 17 total sections, intended or accidental, with

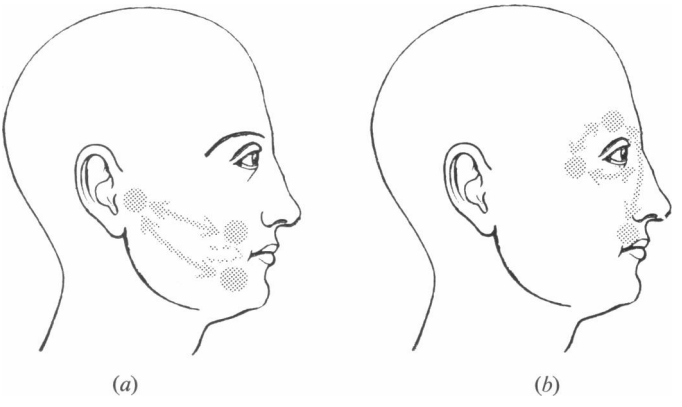


Fig. 15. The principal foci and lines of spread of trigeminal neuralgia. (*a*) In the mouth-ear zone. (*b*) In the nose-orbit zone.

no return of sensation or of pain. The modern intradural approach has eliminated the once-dreaded complication of facial paralysis.

Permanent cure after fractional operations depends mainly upon three anatomical factors. First, when the sensory root is short its most lateral bundle may be hidden under the petrosal sinus and is easily missed, resulting in partial sparing of mandibular sensation (in 18 per cent of 121 lateral section operations), and perhaps recurrence of pain as happened in seven patients; if pain returns the remaining sensation is easily abolished by cutting the sensory root in the posterior fossa. There is rarely any difficulty in seeing clearly the medial border of the sensory root in the middle fossa, but for lateral fractional section the posterior fossa approach, cutting the presenting part of the nerve, is now preferred.

Secondly, it is important to know from the natural history of the pain where it is likely to spread in the future in order to anticipate the possible

appearance of new foci after minimal root section. This leads to a brief description of the anatomical distribution of the pain. The principal foci and lines of spread are shown in Figure 15. The pain is rarely described as being situated in the skin, except perhaps on the forehead and upper lip, and it does not follow the nerves (its distribution corresponds to the lines of the embryological facial clefts). It is a deep pain occurring in the gums, the tongue and deeply in front of the ear (Fig. 15*a*); or at the front of the upper gum (pre-maxilla), deeply up the side of the nose and around and

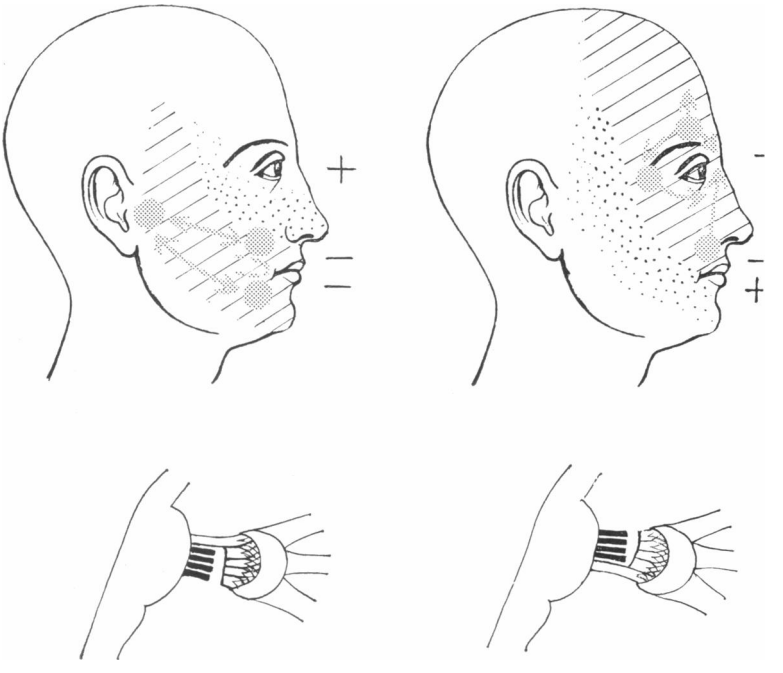


Fig. 16. The operations of fractional sensory root section. Above, the areas of total and partial sensory loss (+ and – indicate sensation on the eye and the gums); below, the amount of sensory root cut and the degenerated root bundles (black). On the left, lateral fractional section; on the right, medial section.

behind the eye socket (Fig. 15*b*). Pain rarely occurs in all three divisions. In 95 per cent of patients it remains confined either to what may be called the mouth-ear zone or to the nose-orbit zone; it is twice as common in the mouth zone.

Although pain may have been limited to one division, e.g. the lower gum or the eyebrow, it is essential to denervate the whole zone in order to prevent pain appearing after several years elsewhere within the same zone, due presumably to gradual extension of the underlying pathology (as normally happens before treatment). This was not fully appreciated

during the earlier years, and pain, that could have been prevented, sometimes appeared at a new focus several years after fractional section that had been restricted to one division instead of including the whole zone; this is commonly seen between the eyebrow and the front of the upper gum. It is therefore necessary to produce total sensory loss in two divisions, i.e. always on the upper gum (the cheek is less important), and in either the first or third division (Fig. 16). When pain is limited to the upper gum fractional operation should be delayed until the pain spreads either up the nose or backwards along the gum to indicate whether medial or lateral section is required. The more conservative middle fractional section, leaving one bundle on each side of the nerve root to preserve a little useful sensation on the eye and in the mouth, is apt to be followed later by the appearance of pain in the first or third division; nevertheless, it is sometimes useful, e.g. when pain is bilateral.

Thirdly, the re-arrangement of nerve fibres in the sensory root plexus, close to the posterior border of the ganglion, results in slight overlap of root bundle supply to each division; this necessitates, as is well known, cutting at least four-fifths of the bundles to be sure of anaesthetizing completely two divisions. It also results in a marginal zone of partial sensory loss and frequently slight impairment of all remaining sensation. If more than one medium-sized bundle is spared, especially on the medial side of the root (because the ophthalmic nerve is smaller than the mandibular), there may be only partial sensory loss on the upper gum, as had occurred in 16 of the 24 patients with recurrence of pain. Sensation never returns after operation, but a focus that still has partial sensation, e.g. on the upper gum, may remain dormant for several years, until the underlying pain stimulus becomes strong enough to cause recurrence of pain at the partially anaesthetic original focus, as happened in eight patients after seven to nine years.

Pain does not spread from one zone to the other, but in 5 per cent of patients a new focus appeared independently in the other zone (in 1.5 per cent of patients similar pain occurred also in the glossopharyngeal area). This usually happened before treatment, but in one patient it occurred five years after fractional section. The incidence of bilateral pain was also 5 per cent, so that when pain starts, for example, in one side of the mouth, it is just as likely to appear later on the other side of the face as in the upper zone on the same side, which is one reason why fractional operations are preferred to total. At the onset of trigeminal neuralgia, treatment should be based on the expectation that the pain may eventually spread to the whole zone, and this should be prevented by adequate fractional section as soon as possible, i.e. during the second attack or a continuing severe first attack, before the patient becomes unfit for operation. The pain should be regarded as bigeminal and not trigeminal, and it may reasonably

be accepted that in the rare event of pain appearing later in the other zone it will be treated separately.

Recurrence of pain after fractional operations was thus due to cutting insufficient root bundles, either because of difficulty in seeing clearly the lateral border of the root in the middle fossa, or because of wrongly sparing too many root bundles allowing preservation of partial sensation on the upper gum. These errors can be more easily avoided than are the anatomical variations and uncertainties that affect the results of blind Gasserian injections.

Late results of operations were available for 158 patients who were re-examined after 1 to 16 years. Pain recurred in 24 patients (15 per cent); only five were early failures with continuation or return of pain within 12 months, and in eight patients recurrence was delayed seven to nine years (whilst 51 patients remained free of pain for 9 to 16 years).

CONCLUSIONS

In a follow-up of patients with trigeminal neuralgia, in whom treatment was intended to produce permanent cure, it was found that operations on the sensory root, which is cut under vision, gave better results than Gasserian ganglion injections which are necessarily rather blind and uncertain.

Both procedures had been carried out in a conservative manner, in that usually only part of the nerve root was cut in order to preserve as much sensation as possible, or, in order to avoid nerve palsies, alcohol was injected only just deep enough to obtain total trigeminal sensory loss in the belief that the needle was then in the ganglion and the result would be permanent. Sensation frequently returned, however, after these supposedly Gasserian injections but never after operation.

In trying to discover why pain sometimes returned after operation, it became evident that failures were due mainly to lack of proper appreciation of the anatomical behaviour of trigeminal neuralgia, with the result that sometimes insufficient nerve root had been cut to allow for possible future spread of the pain. It is necessary to denervate completely two divisions, however localized the pain, to prevent recurrence that sometimes started as late as seven to nine years after operation.

It is believed that after Gasserian injection, the surprising frequency of mandibular regeneration, and also of sensory recovery in all divisions, resulted from alcohol having been injected in front of the ganglion. Post-mortem dissections showed considerable variation in the antero-posterior position of the ganglion; also, that it was very difficult to enter the needle into the medial part of the ganglion, in spite of which, in patients, permanent anaesthesia was more often produced in the first two divisions than in the third.

Post-mortem injections of coloured alcohol showed that it often went medially in front of the ganglion, in a dural emisary venous sinus between the cavernous sinus and the foramen ovale. Alcohol inside the sinuses penetrated the maxillary and ophthalmic nerves and stained the surface of the adjoining medial part of the ganglion. Penetration of dye into ganglion cells was easily demonstrated histologically after injection into Meckel's cave, but not from the venous sinus. It is, however, believed that alcohol in the venous sinus affects the medial part of the ganglion indirectly through the ophthalmic and maxillary nerves, either by extending along their fascicles, or, more likely, by an irreparable retrograde effect from their junction with the ganglion; either mechanism would explain the frequent strictly peripheral nerve distribution of permanent sensory loss in the first two divisions only. The venous sinus passes downwards through the foramen ovale to join the pterygoid venous plexus, and when, in patients, the needle enters it during mandibular nerve injections the same effects sometimes occur as during incomplete Gasserian injections.

The late results would probably have been better than they were if deeper injections into the sensory root, after withdrawing cerebro-spinal fluid from Meckel's cave, had always been attempted, although they are not always possible; and if, during operations, sufficient sensory root had always been cut to anaesthetize two divisions. The overall results were worst in patients with third division pain, in whom Gasserian injections most often failed; and in whom occasional anatomical anomalies make middle fossa operations probably less reliable than the posterior fossa approach which is now preferred for cutting the lateral part of the root.

Permanent cure is more certain, and should almost always be obtained, after operation than after Gasserian injection, but the slight risk of operative fatality has always to be considered when the patient's general condition is poor. It has been generally accepted for many years that the risk can be reduced to less than 1 per cent by selection and early operation while the patient is still fit for anaesthesia; otherwise Gasserian injection is a second best alternative.

There is no single treatment for all cases of trigeminal neuralgia. Some patients will not tolerate injection and others are afraid of operation. There are individual considerations in every case and the best treatment may be operation, or Gasserian injection, or peripheral nerve injection, or tablets; all should be considered in the light of the surgeon's experience with all methods.

ACKNOWLEDGEMENTS

This study owes much to the example of Professor N. M. Dott's high standard of clinical recording which stimulated my interest in trigeminal neuralgia when I reviewed his series in 1938.

It is a great pleasure to thank Dr. D. G. F. Harriman, neuropathologist, to whom I am especially indebted for very valuable suggestions and advice and for his active help with histology. I also wish to thank Professor C. E. Lumsden for facilities in the post-mortem room; Dr. J. A. Sharp, Department of Anatomy, for his interest and helpful discussion; and all former assistants for their case-records. Finally I must thank all patients and their doctors for their very willing co-operation in obtaining follow-up information.

HOLIDAY LECTURES FOR YOUNG PEOPLE

A PROGRAMME OF lectures and demonstrations suitable for young people has been arranged to take place during the Christmas school holidays, as on previous occasions. The lectures and demonstrations are designed to be of interest for those between the ages of 12 and 18, and, although entry will not be strictly limited to this age-group, priority will be given to young people.

PROGRAMME

Tuesday, 4th January 1966

2.00 p.m.	*Tour of the Hunterian Museum.
3.00 p.m.	" The influence of eye diseases on pictorial art." Lecture by Mr. P. D. Trevor-Roper, F.R.C.S.
4.00 p.m.	Tea.
4.30 p.m.	*Tour of the Hunterian Museum.

Wednesday, 5th January 1966

2.00 p.m.	*Tour of the Hunterian Museum.
3.00 p.m.	" X-rays, Ancient and Modern." Lecture by Professor C. B. Allsopp, M.A., Ph.D., D.Sc., F.Inst.P.
4.00 p.m.	Tea.
4.30 p.m.	*Tour of the Hunterian Museum.

Friday, 7th January 1966

2.00 p.m.	*Tour of the Hunterian Museum.
3.00 p.m.	" The Romance of Surgery—The Pillars of Surgery." Lecture by Professor A. L. d'Abreu, O.B.E., F.R.C.S.
4.00 p.m.	Tea.
4.30 p.m.	*Tour of the Hunterian Museum.

* Tours of the Hunterian Museum will be restricted to parties of twenty.

Applications for tickets should be sent to Mr. R. S. Johnson-Gilbert, Secretary, at the College.

LISTER'S WRITINGS

IN THIS CENTENARY year of antisepsis Messrs. E. and S. Livingstone have published *A List of the Original Writings of Joseph, Lord Lister, O.M.*, compiled by the Librarian of the College, Mr. William LeFanu. This list records all Lister's writings as they were first published from 1853 to 1909, and refers to the relevant manuscripts which Lister bequeathed to the College. The pamphlet is on sale through the booksellers or from the Librarian at the College, price 3s. 6d.